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## SCIENTIFIC ARTICLE

# Ilioinguinal-Iliohypogastric Nerve Block with Intravenous Dexketoprofen Improves Postoperative Analgesia in Abdominal Hysterectomies

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Nerve Block;  
Morphine.

### Abstract

**Background and objective:** In this study, our aim was to evaluate the effects of intravenous dexketoprofen trometamol with ilioinguinal and iliohypogastric nerve block on analgesic quality and morphine consumption after total abdominal hysterectomy operations.

**Methods:** We conducted this randomized controlled clinical study on 61 patients. The study was conducted in the operation room, post-anesthesia care unit, and inpatient clinic. We randomly grouped the 61 patients into control group (group C), block group (group B) and dexketoprofen-block group (group DB). Before the skin incision performed after anesthesia induction, we performed ilioinguinal iliohypogastric block (group C given saline and group P and DB given levobupivacaine). In contrast to group C and B, group DB was given dexketoprofen. We administered morphine analgesia to all patients by patient-controlled analgesia (PCA) during the postoperative 24 hours. We recorded Visual Analogue Scale (VAS), satisfaction scores, morphine consumption and side effects during postoperative 24 hours.

**Results:** We found the DB group's VAS scores to be lower than the control group and block group's ( $p < 0.05$ ) values at postoperative 1<sup>st</sup>, 2<sup>nd</sup>, 6<sup>th</sup> and 12<sup>th</sup> hours. VAS scores of group C were higher than of group B at postoperative first 2 hours. Time to first PCA demand was longer, morphine consumption values were lower and satisfaction scores were higher in group DB than in the other two groups ( $p < 0.05$ ).

**Conclusions:** Ilioinguinal-iliohypogastric nerve block with IV dexketoprofen increases patient satisfaction by decreasing opioid consumption, increasing patient satisfaction, which suggests that dexketoprofen trometamol is an effective non-steroidal anti-inflammatory analgesic in postoperative analgesia.

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## Introduction

Despite having advances in the pathophysiology and treatment of pain using novel drugs and complex drug administration systems, many patients still receive treatments that are insufficient for postoperative pain <sup>1,2</sup>. Insufficient treatment of postoperative pain causes patient suffering along with additional morbidity factors and increased costs by preventing early mobilization <sup>1,3,4</sup>.

The mainly used drugs to prevent postoperative pain are the opioid analgesics, non-opioid analgesics and local anesthetic agents <sup>4,5</sup>. Opioid analgesic drugs are the most commonly used drugs in this aspect. However, although they provide highly effective analgesia, the inability to use optimum doses due to risk of addiction and side effects leads to insufficient postoperative analgesia <sup>2,6</sup>. Today, the use of balanced analgesia has become important to increase efficiency of postoperative pain treatment and reduce side effects of drugs especially those of opioids <sup>7-9</sup>. For this purpose, combining opioids with techniques where non-steroid anti-inflammatory drugs or local anesthetics are used have produced a decrease in opioid-related side effects and an increase in analgesic quality <sup>10</sup>. Local anesthetics are used in pain treatment through infiltration, plexus and peripheral nerve blocks, intercostal block, epidural block and subarachnoid block <sup>4</sup>. Methods where local anesthetics are infused into the surgical site have recently been used in various surgeries, as they are practical, easy to apply and provide effective analgesia <sup>11</sup>. Promoting a conduction block in iliohypogastric and ilioinguinal nerves by using local anesthetics is effective in relieving somatic pain of Pfannenstiel incision. However, as visceral pain cannot be relieved by blockade of these nerves, additional analgesia modalities are needed. The most common and effective method is using opioids. However, opioids are of concern because of their adverse effects such as itching, nausea, vomiting, constipation, sedation, respiratory depression and addiction potential. The main analgesic strategy is to minimize the dose of opioid in order to reduce or eliminate these adverse effects <sup>11</sup>.

Dexketoprofen trometamol is an active enantiomer of ketoprofen and has been shown to be more potent with less gastrointestinal side effects when compared to ketoprofen. It has been used in osteoarthritis, dysmenorrhea and dental and orthopedic surgery and found to be highly effective <sup>12</sup>.

In the present study, our aim was to evaluate the effect of ilioinguinal and iliohypogastric nerve block alone and combined with IV dexketoprofen trometamol on analgesic quality. Primary outcomes are morphine consumption, pain score and satisfaction scores; secondary outcomes are opioid-related side effects. We hypothesized that intravenous dexketoprofen would improve analgesic quality of ilioinguinal and iliohypogastric nerve block, decreasing morphine consumption.

## Material and Methods

The present study was conducted on 66 patients (ages between 30-65 years old) in the American Society of Anesthesiologists (ASA) I-II risk group and undergoing elective total abdominal hysterectomy and/or bilateral

salpingo-oophorectomy, after getting approval from the Ethical Committee (Decision No: 2009-12/22) and written informed consent from the patients. Exclusion criteria were: hypersensitivity or history of allergy to the amid local anesthetics, to opioid and dexketoprofen trometamol, history or suspicion of opioid drug use, renal, cardiac and liver function disorders, coagulation disorder, pathological obesity (body mass index > 35), sepsis, non-regulated hypertension and diabetes, history of convulsion or neurologic disorder, gastrointestinal ulcer, ulcerative colitis, Crohn's disease, chronic dyspepsia, having an operation longer than 120 minutes, being in a cultural and mental state that prevents using patient controlled analgesia (PCA) equipment and the patient's refusal of being included in the study. Our study was controlled, randomized and double blind. During the visit one day before the operation, we obtained patients' oral and written consents by explaining to them how to use 10 cm visual analogue scale (VAS) and PCA equipment. No premedication was given to the patients. We achieved fluid replacement during surgical intervention by lactated Ringer's infusion at a rate of 10 mL.kg<sup>-1</sup> for the first hour and 5 mL.kg<sup>-1</sup> for the following hours. When the patients were taken to the operation room, we recorded electrocardiography (ECG), heart rate (HR), pulse oximetry (SpO<sub>2</sub>) and mean arterial pressure (MAP) monitoring (Dräger, Infinty® Vista XL, USA) at preoperative baseline, after induction, 1 minute after intubation, at surgical incision and at 10-minute intervals during the operation. In all the cases, we achieved anesthesia induction with 1 µg.kg<sup>-1</sup> fentanyl (Fentanyl citrate, Abbot, USA), 0.5 mg.kg<sup>-1</sup> rocuronium (Esmeron®, Organon, Holland) and 5-7 mg.kg<sup>-1</sup> thiopental (Ekipental, Tum Ekip, Turkey). We managed anesthesia using 1-2% sevoflurane (Sevorane likid®, Abbott, USA) in 50% O<sub>2</sub> and 50% N<sub>2</sub>O mixture. We randomly grouped patients as the control group (group C), block group (group B) and dexketoprofen-block group (group DB) by the sealed envelope technique. Each group consisted of 22 patients. An anesthesiologist who was blinded to study groups performed randomization in the operating room and another anesthesiologist blinded to the study groups prepared all solutions for study injections. Before the skin incision performed after anesthesia induction, the same anesthesiologists performed ilioinguinal iliohypogastric block by advancing the needle perpendicular to the skin at a point 2 cm medial and 2 cm superior to the spina iliaca below the fascia of the external oblique muscle by loss of resistance method. Then, the anesthesiologist withdrew the needle from the skin and redirected it at 45-degree angles superior and inferior to the previous point until a loss of resistance was felt. In the control group patients, the team injected 4 mL saline to the case in the control groups while 4 mL 0.5% levobupivacaine (Chirocaine® 0.5%, Abbott, USA) was administered to the cases in the block group and dexketoprofen-block group. Five minutes after anesthesia induction, the team administered IV 1 mL saline as placebo to the cases in the control and block group while they administered IV 25 mg dexketoprofen trometamol to the cases in the dexketoprofen-block group. In all the groups, we repeated IV doses twice at an 8-hour interval based on the first administration time. We tested the block's success using the pinprick test and we regarded patients having no bilateral or unilateral sensory

loss as unsuccessful block and excluded them from further evaluations. Patients were taken to post-anesthesia care unit (PACU) after the operation. We administered morphine analgesia by PCA equipment (GemStar®, Abbott Hospira, USA) to all the patients during postoperative 24 hours. We adjusted the PCA equipment so that the concentration and bolus dose was 1 mg before administering loading dose and hourly infusion; lockout interval was 20 minutes and 4-hour limit was 20 mg. We recorded side effects such as itching, nausea and vomiting, sedation, respiratory depression, bradycardia and hypotension. We also recorded time to first PCA demand, total morphine consumption over 24 hours and patient satisfaction scores. We recorded nausea and vomiting as well. We evaluated severity of pain using 10 cm VAS (0: far left end indicated "no pain" and 10: the far right end indicated "severe pain"). We measured patient satisfaction using a 4-point scale (1: totally unsatisfied, 2: moderately satisfied, 3: satisfied, 4: totally satisfied). If the patient had nausea, we administered antiemetic (metoclopramide) at least every 6 hours and recorded it. The staff, blinded to study groups, recorded all postoperative data.

### Statistical evaluation

We performed a power analysis using a pilot study: 20 patients scheduled for elective abdominal hysterectomies under general anesthesia consumed a mean  $\pm$  SD of  $27 \pm 9$  mg of morphine in the first 24 h with a PCA pump. To achieve a 25% reduction of opioid consumption with  $\alpha$  error of 0.05 and power of 80%, the study needed 22 patients in each group. We loaded the present study's data into SPSS (Version 14.0) and used Kolmogorov Smirnov test and normality test to evaluate the data. We carried out a variance analysis with the ANOVA and Kruskal Wallis tests. We used Mann Whitney U and Friedman tests for intergroup continuous variables with irregular distribution. We used the Wilcoxon test for intragroup comparison of parameters with irregular distribution. We used the Chi-square test to compare quantitative

data. The tables below show our data as arithmetic mean  $\pm$  standard deviation and number and percentage of subjects. We determined the statistical significance as 0.05.

### Results

We excluded two patients from group DB ( $n = 20$ ) and 3 patients from group B ( $n = 19$ ) due to unsuccessful block. Therefore, a total of 61 patients were enrolled in the study. We found no significant difference when patients were undergoing elective abdominal hysterectomy in terms of operation and demographic features such as age and weight (Table 1).

When we compared MAP and HR values, we found differences in all measurements to be insignificant between groups. We found a statistically significant difference when we compared HR data ( $p < 0.05$ ).

When we compared VAS scores, we found values of the dexketoprofen-block group to be lower than the values of the control group and block group ( $p < 0.05$ ) at postoperative 1<sup>st</sup>, 2<sup>nd</sup>, 6<sup>th</sup> and 12<sup>th</sup> hours. VAS scores of control group were higher than of block group at postoperative first 2 hours (Figure 1).

When we compared the groups in terms of time to first analgesic demand and morphine consumption amounts, we found the difference among the groups to be significant ( $p < 0.05$ ). When compared to the control and block groups, we found the dexketoprofen-block group (DB) to be lower in terms of morphine consumption ( $p < 0.05$ ). Furthermore, we found morphine consumption value of group B to be lower than group C ( $p < 0.05$ ). When we compared the groups in terms of the time to first analgesic demand, we found the dexketoprofen-block group to be significantly higher than the control group and the block group ( $p < 0.05$ ) and block group to be higher than the control group (Table 2).

When we compared patient satisfaction scores, we found the difference among the groups to be significant ( $p < 0.05$ ). The ratio of overall satisfaction score statements 24 hours

**Table 1 - Demographic data.**

	Group C (n = 22)	Group B (n = 19)	Group DB (n = 20)
Age (year)	44.8 $\pm$ 12.0	47.2 $\pm$ 7.9	48.2 $\pm$ 8.8
Weight (kg)	65.4 $\pm$ 12.1	65.3 $\pm$ 12.8	69.9 $\pm$ 13.3
Height (cm)	160.3 $\pm$ 12.5	164.7 $\pm$ 10.9	167.1 $\pm$ 9.2
Duration of operation (min)	75.6 $\pm$ 18.9	83.3 $\pm$ 19.7	78.8 $\pm$ 23.3
ASA I/II (n)	7/15	6/13	8/12

**Table 2 - Postoperative data.**

	Group C (n = 22)	Group B (n = 19)	Group DB (n = 20)
Morphine consumption 24 hours (mg)	27.1 $\pm$ 9.9	14.3 $\pm$ 8.7 <sup>a</sup>	6.1 $\pm$ 3.4 <sup>b</sup>
Time to first PCA (min)*	104.2 $\pm$ 19.1	298.4 $\pm$ 33.8 <sup>a</sup>	526.6 $\pm$ 51.9 <sup>b</sup>
Satisfaction score	1.7 $\pm$ 0.7	2.9 $\pm$ 1.1 <sup>a</sup>	3.7 $\pm$ 1.3 <sup>b</sup>
Nausea (+/-)	5/17	3/16	2/18
Vomiting (+/-)	0/22	0/19	0/20
Itching (+/-)	4/18	3/16	2/18

<sup>a</sup> $p < 0.05$  when compared to group C and group DB; <sup>b</sup> $p < 0.05$  when compared to group C and group B; \*calculated from transferring time to PACU.

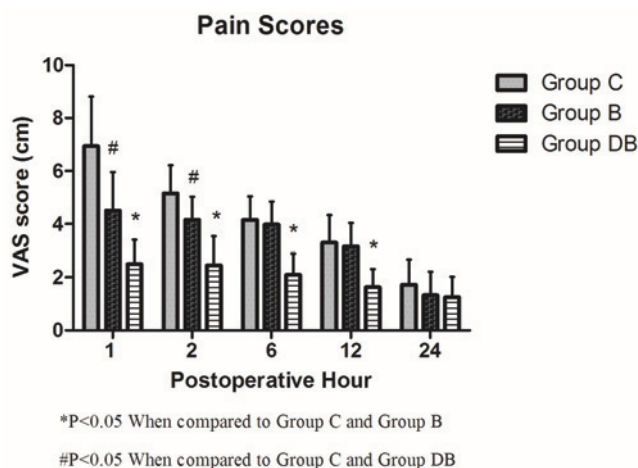


Figure 1 VAS Pain Scores.

after the operation was higher in group DB than group C and B ( $p < 0.05$ ). Similarly, satisfaction score of group B was higher than that of group C ( $p < 0.05$ ). There were no differences between groups concerning nausea, vomiting and itching.

## Discussion

According to our literature review, the analgesic effectiveness of ilioinguinal iliohypogastric block and dexketoprofen trometamol combined in the treatment of postoperative pain after elective abdominal hysterectomies has not been studied before. We found postoperative total morphine consumption and time to first analgesic demand to be significantly lower in the dexketoprofen-block group, compared to the control and block groups. We found resting VAS values obtained during postoperative period to be low in the dexketoprofen-block group in all time points.

Kehlet et al.<sup>7</sup> stated that multimodal analgesia was the combination of different analgesics that act through different mechanisms, resulting in an additive or synergistic effect. Through different combinations, a successful analgesia could be obtained by lowering the doses of drugs from each group and decreasing the frequency of the side effects<sup>7</sup>. We prefer methods where local anesthetics are infiltrated into the surgical site as they are practical, easy to apply and provide effective analgesia<sup>10</sup>. Combining opioids with techniques where non-steroid anti-inflammatory drugs or local anesthetics are used decrease opioid-related side effects and increase analgesic quality<sup>10</sup>. In a prospective study of 61 patients undergoing laparotomy under anesthesia, Wehbe et al.<sup>13</sup> created bilateral ilioinguinal-iliohypogastric nerve block by bupivacaine + epinephrine injection 5 minutes before the first skin incision and after closure of fascia. They evaluated VAS values, average amount of morphine consumption, side effects (itching, nausea, vomiting), duration of hospitalization and patient satisfaction and found no difference between the two groups. However, Wehbe et al.<sup>13</sup> suggested that the ilioinguinal iliohypogastric nerve blocks were not performed by the same surgeon, which could be the reason they did

not obtain any effective result by ilioinguinal iliohypogastric nerve block<sup>13</sup>. In our study, the same surgeon performed all surgery procedures.

In a similar study on patients undergoing hysterectomy with ilioinguinal iliohypogastric nerve block, Oriola et al.<sup>14</sup> found a 50% decrease in morphine consumption during the first postoperative 48 hours. However, in terms of pain scores, they could not find any difference between the block group and control group. In our study, the dexketoprofen-block group was the group having lower scores in terms of opioid consumption and VAS and the highest scores in terms of patients' satisfaction. In terms of side effects, there was no significant difference among the groups.

In a study where researchers compared efficiency of ilioinguinal-iliohypogastric nerve block and lower intercostal nerves blockade in patients undergoing renal transplantation, Shoeibi et al.<sup>15</sup> found through median VAS scores that the average amount of morphine consumption was  $12.7 \pm 10.5$  mg in the block group and  $34.9 \pm 5.9$  mg in the control group ( $p < 0.05$ ). Similarly, there was a difference among the groups in terms of morphine consumption and VAS scores in our study too, which indicates that the blocks were successful in both of these studies.

Huffnagle et al.<sup>16</sup>, studied ilioinguinal iliohypogastric nerve blocks before or after cesarean delivery under spinal anesthesia. According to the results obtained by Huffnagle et al.<sup>16</sup>, there was no benefit to ilioinguinal iliohypogastric nerve blocks, either before or after surgery, in patients receiving spinal anesthesia for elective cesarean delivery. The reasons for the unsuccessful blocks were related to the fact that caesarean surgery pains were primarily caused from the visceral pain due to contractions of the uterus. Results of the said study are not similar to the results of our study performed on patients undergoing hysterectomy under general anesthesia. When we compared postoperative efficiency of the nerve block before surgery with the control group, we found that morphine consumption decreased and patient satisfaction increased in the block group. Although somatic pains due to Pfannenstiel incision in the abdominal wall are prevented by ilioinguinal iliohypogastric block, it is clear that this would not be effective for the visceral component of postoperative intra-abdominal pains. Thus, these blocks may only partially decrease the amount of opioid used.

Studies have shown that a non-opioid agent combined with these blocks would significantly increase the amount of opioid used<sup>17</sup>. Mc Gurk et al.<sup>18</sup> found that the analgesic effect of dexketoprofen started in 30 minutes, while effects of ketoprofen had a late onset. In a study comparing 50 mg dexketoprofen and 100 mg ketoprofen after orthopedic surgery, Iohom et al.<sup>19</sup> found that opioid consumption and pain scores were lower in the dexketoprofen group. In their study on animals, Cabre et al.<sup>20</sup> concluded that the analgesic and anti-inflammatory effect was at least twice as potent as ketoprofen. Adding trometamol to dexketoprofen (36.9 mg) increased solubility and sped oral absorption compared to free acid form. Maximum concentration (Cmax) is reached approximately 30 minutes after oral administration and does not cause accumulation in repeated administrations as its elimination is rather fast. The advantages of dexketoprofen



trometamol over ketoprofen include having a more rapid onset, being more potent and having fewer adverse gastrointestinal effects. It has been used in osteoarthritis, dysmenorrhea and dental and postoperative analgesia and found to be highly effective <sup>19</sup>. In a recent study, Jamdade et al. <sup>8</sup> stated that a single dose of dexketoprofen trometamol 50 mg given intramuscularly provided faster, better, and longer duration of analgesia in postoperative patients of hernia repair surgery compared to diclofenac 50 mg, with comparable safety.

Gaitan et al. <sup>21</sup> concluded that the combination of fentanyl and sub-effective doses of dexketoprofen trometamol induced a more potent and longer lasting analgesic effect than that observed with fentanyl alone, and that this was not an opioid-mediated action <sup>20</sup>. In our study, we found that adding dexketoprofen trometamol IV to ilioinguinal-iliohypogastric nerve block decreased the amount of analgesic consumed. We believe multimodal analgesia leads to more efficient balanced results in postoperative pain control. Hanna et al. <sup>22</sup> studied non-steroidal anti-inflammatory drugs (NSAIDs) and opiates combined, resulting in synergistic analgesia by acting through different mechanisms. The study was aimed at assessing the analgesic efficacy, relative potential and safety of dexketoprofen trometamol following major orthopedic surgeries by maintaining that there were few parenteral administered NSAIDs. We randomly divided 172 patients that would undergo elective surgery into three groups, and the first group received IM 50 mg dexketoprofen, the second group, 100 mg ketoprofen and the third group received 0,9% NaCl (12 hourly). The mean cumulative amount of morphine used via PCA was 39 mg in the dexketoprofen group and 45 mg in the ketoprofen group, versus 64 mg in the placebo group. The differences were statistically significant. Pain scores were lower compared to the control group and the lowest pain scores were in dexketoprofen group <sup>22</sup>. Similarly, in our study, VAS values and morphine consumption were the lowest in the dexketoprofen-block group. Having no difference among our patients in terms of nausea and vomiting as side effects suggests opioids are the most important factors leading to increases in nausea and vomiting. In PCA, this ratio reaches above 50% with morphine usage. Ng and Smith et al. <sup>23</sup> adjusted PCA equipment to a bolus dose of 1 mg and lockout interval of 5 minutes, as in our study. Although they found morphine consumption in 24 hours to be 54 mg in the parecoxib group and 72 mg in the control group, they found the difference between the groups in terms of nausea-vomiting episodes and antiemetic usage to be insignificant.

Finally, we have come to the conclusion that ilioinguinal-iliohypogastric nerve block in abdominal hysterectomy operations increases patient satisfaction and analgesia by decreasing opioid consumption without negatively affecting intraoperative hemodynamic during postoperative period; however, using dexketoprofen additionally leads to a significant decrease in postoperative opioid consumption and significant increase in patient satisfaction, which suggests that dexketoprofen trometamol is an effective non-steroidal anti-inflammatory analgesic in postoperative analgesia.

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